Effects of Polygenic Risk and Perceived Friends' Drinking and Disruptive Behavior on Development of Alcohol Use Across Adolescence

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ABSTRACT. Objective: Developmental theory posits interacting individual and contextual factors that contribute to alcohol use across adolescence. Despite the well-documented salience of peer environmental influences on adolescent drinking, it is not known whether peer environments moderate polygenic risks for trajectories of alcohol use. The current theoretically based investigation aimed to test developmental gene–environment interaction (G×E) effects across adolescence. **Method:** Latent growth curve models tested interactive associations of polygenic risk scores and adolescents' perceived friend drinking and disruptive behavior with adolescents' initial level of alcohol use frequency at age 16 years old and change in alcohol frequency from ages 16 to 20. The sample comprised 8,941 White adolescents (49% female) from Great Britain within the Avon Longitudinal Study of Parents and Children (ALSPAC). **Results:** Greater polygenic risk was associated with more frequent initial drinking as well as escalations in drinking frequency over the subsequent 5 years in latent growth curve models. Contrary to study hypotheses, no significant G×E effects were identified after controlling for confounding main and interaction effects. **Conclusions:** Adolescents at heightened genetic risk may accelerate their alcohol use across adolescence, although not significantly more so in the presence of these alcohol-promoting peer environments. Future well-powered, theoretically driven replication efforts are needed to examine generalizability of these findings across diverse samples. (*J. Stud. Alcohol Drugs, 81,* 808–815, 2020)

ADOLESCENCE IS a crucial developmental period for initiation and rapid escalation of alcohol use. More than 37% of adolescents ages 15–19 years old report ever consuming alcohol worldwide, with rates rising to almost 60% in Europe and 70% in North and South America (World Health Organization [WHO], 2018). Once initiated, alcohol use can rise substantially. Rates of binge drinking increased from 4% at ages 14–15 to almost 30% by ages 18–20 in the United States alone (Substance Abuse and Mental Health Services Administration, 2014). Adolescent alcohol use can have far-reaching impacts, contributing to academic/occupational impairment, violence, injury, risky sexual behavior, traffic accidents, and death (Hingson & Kenkel, 2004; Marshall, 2014; Miller et al., 2007).

Developmental theories posit pathways to alcohol use through intersecting individual and contextual factors (Zucker et al., 2016). Interplay between an individual's genetics and their environment can drive actualization of genetic influences on behavior (Zucker et al., 2016). For example, gene–environment interaction (G×E) research examines whether environments moderate the degree to which genetics influence behavioral outcomes (Brendgen, 2012; Rutter et al., 2006). Several models have been proposed for G×E effects in alcohol outcomes. Social control and related frameworks (Chartier et al., 2017; Shanahan & Hofer, 2005) suggest that social contexts may influence manifestation of genetic risks by constraining and/or enabling access to alcohol or opportunities to engage in drinking. Permissive social contexts—such as those with frequent peer drinking, greater community access to alcohol, and less restrictive alcohol policies—may provide opportunities to actualize genetic risks.

Among the many socioenvironments that could modulate genetic risks, peer influences are particularly salient

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in adolescence (Crawford & Novak, 2002). Developmental theory highlights both alcohol-specific and nonspecific risks in alcohol use development (Zucker et al., 2016). Regarding alcohol-specific peer environments, peer drinking predicted escalations in alcohol use from adolescence into young adulthood, after controlling for shared environmental and genetic risks (Cruz et al., 2012). Regarding alcohol nonspecific peer environments, greater perceived affiliation with deviant peers was associated with increased likelihood of subsequent alcohol problems, even after controlling for potential selection into deviant peer networks (Fergusson et al., 2002), and was prospectively associated with adolescent drinking in a systematic review (Leung et al., 2014). From a social control framework, permissive environments with prevalent friend drinking and general disruptive behavior may increase access and exposure to alcohol, provide indirect or overt pressures to drink, contribute to favorable alcohol cognitions, or increase opportunities for externalizing behavior, thereby leading to manifestation of genetic susceptibilities for drinking.

Despite theoretical support for gene–environment interplay in alcohol use development, there has been a comparative lack of empirical developmental G×E research. Such research is necessary to understand whether G×E effects can explain some adolescents' rapid escalations in drinking and whether any environmental modulation may change in salience over time. Limited research into developmental G×E effects has typically focused on candidate genes, similar to the G×E literature more broadly (see Milaniak et al., 2015). Specifically, a dopaminergic gene variant moderated associations of perceived friend drinking with personal drinking across 5 years (Mrug & Windle, 2014), although a composite of dopaminergic variants did not moderate associations of perceived friend drinking with personal alcohol trajectories in another sample (Coley et al., 2017). Possible G×E effects on alcohol use development may be much broader than those captured by candidate gene research, with peer environments modulating genetic susceptibilities across the genome. Composite genetic risk scores model the aggregate impact of genetic variants on behavior (Dudbridge, 2013) and, thus, may permit a more comprehensive understanding of the genetic underpinnings to alcohol use.

Existing literature on peer environmental modulation of composite genetic risks in alcohol use development is limited and mixed. Within a twin study, genetic influences on drinking trajectories differed as a function of friend drinking, with greater genetic influences in the presence of higher friend drinking (n = 842; Zheng et al., 2019). However, two additional investigations with polygenic risk scores of trait-associated variants yielded nonsignificant findings. Polygenic risk scores of alcohol dependence did not moderate associations of perceived friend substance use on heavy episodic drinking from adolescence into emerging adulthood (n = 412; Li et al., 2017) or associations of perceived friend deviant behavior on alcohol use disorder symptom trajectories across college (n = 1,119; Su et al., 2018).

In light of the theoretical support for possible developmental G×E effects, these limited and inconsistent findings highlight the need for future work aimed at resolving current discrepancies. Of note, G×E literature has been subject to concerns over false positive and negative findings arising from statistical concerns in modeling interactions, consideration of confounding effects, and low power (Dick et al., 2015; Duncan & Keller, 2011). Well-powered investigations within large samples are needed to maximize the likelihood of detecting any true, small G×E effects, and such replication efforts should be prioritized (Duncan & Keller, 2011). Further, such work should adequately control for potential confounds to the primary G×E effect of interest (Keller, 2014). When examining peer moderation of genetic risks, it is important to account for the robust sex differences in alcohol use (Erol & Karpyak, 2015) and peer-alcohol relations (Mrug & McCay, 2013) as well as the role of parental drinking in adolescents' genetics and peer environments (Bahr et al., 2005; Jacob et al., 2003). In summary, theoretically driven and well-powered investigations into peer environments modulating genetic risks in development of alcohol use across adolescence are needed to bring clarity to the limited and mixed extant literature.

This project examined interactive associations of polygenic risks and perceived friend environments on the development of drinking across adolescence using a large, prospective sample. Polygenic risk scores were hypothesized to interact with developmentally salient alcohol-specific (i.e., perceived friend drinking) and nonspecific (i.e., peer disruptive behavior) environments in their associations with drinking. Specifically, consistent with a social control framework, it was hypothesized that alcohol-promoting environments would be associated with magnified composite genetic risks for adolescents' initial level of drinking frequency at age 16 as well as their changes in drinking frequency from ages 16 to 20.

Method

Participants

Data were obtained from the Avon Longitudinal Study of Parents and Children (ALSPAC), an ongoing prospective, population-based study (Boyd et al., 2013; Fraser et al., 2013). Pregnant women in the Avon area of Great Britain with an expected delivery date between April 1, 1991, and December 31, 1992, were invited to participate. Mothers, their partners, and their children arising from the index pregnancy were followed up with postal questionnaires and clinic visits. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Please note that the study web-

site contains details of all the data available through a fully searchable data dictionary and variable search tool (http://www.bristol.ac.uk/alspac/researchers/our-data). This study used data from 8,941 ALSPAC children with genome-wide association study (GWAS) data. Because ALSPAC's quality control filtering removed participants of non-European ancestry to avoid population admixtures, this sample was exclusively White.

Measures

Adolescent drinking frequency. Drinking frequency was selected as the main outcome because it has demonstrated better sensitivity and specificity than other indices for adolescent alcohol use disorder symptoms (Chung et al., 2012). Adolescents reported on their drinking frequency at ages 16, 17, 18, and 20 through computerized interviews or postal questionnaires. Adolescents were presented with the definition and/or a visual representation of a drink unit (half pint of average-strength beer, one small glass of wine, or one single measure "shot" of spirits). Adolescents answered, "How often do you usually drink alcohol?" using 0 = *never,* 1 = *monthly or less,* 2 = *2–4 times a month,* 3 = *2–3 times a week,* or 4 = *4 or more times a week.*

Perceived friend drinking and disruptive behavior. Adolescents reported their friends' behaviors through computerized interviews at age 15 using items adapted from the Edinburgh Study of Youth Transitions and Crime (Smith & McVie, 2003). For perceived friend drinking, adolescents answered, "How many of your friends drank alcohol during the last year?" using 0 = *none,* 1 = *one or some,* or 2 = *most or all.* For perceived friend disruptive behavior, adolescents answered 17 items (e.g., "Have any of your friends stolen something?") with 0 = *no* or 1 = *yes,* and a sum score was computed (possible range: 0–17); although not hypothesized to represent a single construct, these items generally clustered together (Cronbach's $\alpha = .86$).

Genetic factors. A complete description of ALSPAC's genetic methodologies is available elsewhere (see Boyd et al., 2013). Polygenic risk scores were generated in ALSPAC using summary statistics from a large GWAS study from the U.K. Biobank (http://www.nealelab.is/uk-biobank). GWAS results were pre-processed to remove strand-ambiguous markers, insertions/deletions, duplicate variant IDs, and markers with low-quality imputation (i.e., INFO < 0.9). Markers in extended linkage disequilibrium regions were restrictively grouped using the --clump command in PLINK ($R^2 > 0.1$, 500 kb physical distance; Purcell et al., 2007). Polygenic risk scores were computed in ALSPAC as a linear score of the number of alleles weighted by their respective β coefficients from the U.K. Biobank GWAS using the --score command (Purcell et al., 2007).

Polygenic risk scores were generated across a range of *p* value thresholds (<.0001, <.001, <.01, <.05, <.10, <.20, <.30, <.40, <.50). All polygenic risk scores were significantly associated with adolescent alcohol use frequency, with the exception of the $p < .0001$ score at age 16. These scores explained 0.1%, 0.4%, 0.4%, 0.6%, 0.6%, 0.6%, 0.7%, 0.7%, and 0.7% of the variance in adolescent alcohol frequency at age 16 and 0.7%, 1.0%, 1.6%, 2.2%, 2.1%, 2.3%, 2.3%, 2.4%, and 2.4% at age 20, respectively. The $p < .50$ score that maximized predicted variance was retained for analyses, with ancillary analyses across the range of scores demonstrating the same pattern of significance for the G×E terms as results below. Principal components analysis was conducted on autosomal markers in low linkage disequilibrium ($R^2 < 0.1$) across a 100 kb window with a 50 variant count step size using the --indep-pairwise command in Plink (Purcell et al., 2007). The first 10 genetic principal components (Price et al., 2006) were included as covariates to adjust for population stratification.

Covariates. Given the potential confounding effects of parents on adolescents' peer environments and genetic risks (Bahr et al., 2005; Jacob et al., 2003), we controlled for maternal and maternal partner's drinking data available in ALSPAC. Mother and mother's partner consumption of six or more units of any alcoholic beverage on any day of the week was recoded into a single variable representing maternal and/or maternal partner heavy drinking (0 = *no;* 1 = *yes*). Further, adolescent male sex (0 = *female;* 1 = *male*) was included as a covariate.

Data analytic strategies

Descriptive statistics. Descriptive statistics and bivariate correlations were conducted in IBM SPSS for Windows, Version 24 (IBM Corp, Armonk, NY). Nonnormality of friend disruptive behavior (skewness = 1.86; kurtosis = 3.70) was addressed by square root transformation (resulting skewness = 0.48; kurtosis = -0.75), with the transformed score used for analyses; all other variables (including adolescent drinking frequency) were approximately normally distributed at each timepoint (skewness = -1.24–1.73; kurtosis = -2.00–2.26). Multivariate normality was examined through Mahalanobis Distance estimates using a chi-square distribution with 15 *df* (for the 15 predictors), and 27 multivariate outliers ($p > .001$) were removed.

Missing data and sensitivity analyses. Maximum likelihood estimation with robust standard errors dealt with missing outcome data by determining the parameters that maximized the probability of the sample data based on available data without imputing missing data (Enders, 2001; Graham et al., 2003). Further, conditional growth curve models specified variances of the exogenous variables to address missing data in the covariates. Sensitivity analyses comparing conditional growth curve models among the full sample to results among participants with complete data (n = 3,295–3,299) yielded the same pattern of significance

Table 1. Means (and standard deviations) or percentages and bivariate correlation coefficients among study variables

	M (*SD*) or %	1.	2.	3.	4.	5.	6.	7.	8.
1. Sex (0 = *female;* 1 = *male*)	51%	–							
2. Parental heavy drinking (0 = *no;* 1 = *yes*)	17%	-.02	–						
3. Polygenic risk score	0.00 (1.62)	-.01	.02	–					
4. Perceived friend drinking (15 years)	1.65 (0.54)	-.06***	.03	.03*	–				
5. Perceived friend disruptive behavior (15 years)	0.92 (0.89)	.10***	.04*	.02	.33***	–			
6. Adolescent drinking frequency (16 years)	1.63 (0.90)	.03	.06***	.09***	.29***	.24***	–		
7. Adolescent drinking frequency (17 years)	1.90 (0.91)	.09***	.06**	.08***	.27***	.19***	.55***	–	
8. Adolescent drinking frequency (18 years)	2.22 (0.98)	.11***	.03	.11***	.21***	.12***	.42***	.54***	–
9. Adolescent drinking frequency (20 years)	2.16 (0.94)	.13***	.04	.16***	.14***	.08***	.33***	.40***	.49***

Notes: N = 1,778–8,905, because of missing data. Spearman's ρ reported for correlations involving ordinal variables, and biserial correlations reported for correlations involving a continuous and dichotomous variable. Polygenic risk score results reported here are based on a $p < .50$ threshold, which was found to maximize predicted variance in adolescent drinking frequency; ancillary analyses across the range of polygenic risk score thresholds are available through author request. Regarding perceived friend drinking, 3% of adolescents endorsed "none," 28% endorsed "one or some," and 68% endorsed "most or all."
*$p < .05$; **$p < .01$; ***$p < .001$.

as results presented below, except Parental Drinking × Polygenic Risk score became significant in peer disruptive behavior models (b = -0.04, p = .046). Compared to those with incomplete data (n = 5,267), participants with complete data on all exogenous variables (n = 3,647) were more likely to be female, $\chi^2(1) = 24.40$, $p < .001$, have greater polygenic risk, $t(8930) = 5.57$, $p < .001$, and report lower friend drinking, $t(1152.32) = -2.35$, $p = .02$, yet greater personal drinking at age 18, $t(2592) = 2.39$, $p = .02$, and at age 20, $t(3247) = 4.50$, $p < .001$.

Unconditional latent growth curve models. Latent growth curves of drinking frequency from ages 16 through 20 were estimated in Mplus, Version 7.4 (Muthén & Muthén, 2012). Alcohol use frequency indicators were specified as categorical outcomes. An unconditional latent growth curve model was fit to determine whether significant heterogeneity existed in drinking frequency. The unconditional latent growth curve model estimated two latent growth factors: an intercept (i.e., the mean alcohol frequency at age 16) and a linear slope (i.e., the average rate of yearly linear change in alcohol frequency from ages 16 through 20), as well as variability within these factors. Factor loadings for the intercept were set to 1, and factor loadings for the slope were set to 0, 1, 2, and 4 to represent measurement intervals by years for the alcohol use frequency indicators.

For the parameterization of the growth model for the categorical indictors, the mean of the latent intercept growth factor was fixed at zero (Muthén & Muthén, 2012). The quadratic growth factor was dropped because reductions in Akaike information criterion (AIC) and sample-size adjusted Bayesian information criterion (aBIC) were comparatively greater (2.5×) for the addition of a linear slope to the intercept-only model compared with the addition of a quadratic growth term to the intercept with linear slope model. Significant variance in the initial level (i.e., intercept) and/or rate of linear change over time (i.e., linear slope) was interpreted to support subsequent conditional growth curve models.

Conditional latent growth curve models. Conditional latent growth curves examined associations of genetics, peer environments, and their interaction on the latent intercept and linear slope factors. Separate models were tested for perceived friend drinking and disruptive behavior. Predictors and covariates were mean centered before calculating product terms, and two-way interactions of each covariate (i.e., sex, parental heavy drinking, genetic principal components) with the genetic and environmental predictors were included to control for any confounding interaction effects (Keller, 2014). Exogenous covariances involving principal component covariates were fixed at zero to allow for model convergence. Any significant interactions of polygenic risk score with perceived friend environments indicated G×E effects on adolescents' initial level and/or rate of change in drinking frequency over time.

Results

Descriptive statistics

Means (and standard deviations) or percentages and bivariate correlations among study variables are shown in Table 1. On average, adolescents reported increasing their drinking frequency over time, from approximately monthly or less at age 16 (M = 1.63, SD = 0.90) to 2–4 times a month at age 20 (M = 2.16, SD = 0.94). Greater perceived friend drinking and disruptive behavior at age 15 were significantly associated with more frequent personal drinking (rs = .08–.29, $p <$ .001).

Unconditional latent growth curve models

Unconditional latent growth curves indicated significant increases in alcohol use frequency over time (b = 0.44, $p <$ .001) as well as significant variance in the initial level of alcohol frequency at age 16 (b = 4.64, $p < .001$) and in its rate of change over time from ages 16 through 20 (b = 0.21, $p <$ .001). This significant heterogeneity supported subsequent conditional latent growth curve models to examine predictors of such heterogeneity.

TABLE 2. Conditional latent growth curve models of associations of polygenic risk score, perceived friend environments, and their interaction on adolescent drinking frequency from ages 16 through 20 years old

	Intercept				Slope			
Variable	*b*	*SE*	β [95% CI]	*p*	*b*	*SE*	β [95% CI]	*p*
Model 1: Perceived friend drinking								
Sex (0 = *female;* 1 = *male*)	**0.11**	**0.03**	**0.08 [0.04, 0.11]**	**<.001**	**0.05**	**0.01**	**0.15 [0.09, 0.22]**	**<.001**
Sex × Polygenic Risk Score	0.02	0.02	0.02 [-0.02, 0.05]	.36	0.00	0.01	0.01 [-0.06, 0.07]	.79
Sex × Friend Drinking	**0.05**	**0.02**	**0.06 [0.01, 0.10]**	**.01**	**-0.02**	**0.01**	**-0.09 [-0.16, -0.02]**	**.01**
Parental drinking (0 = *no;* 1 = *yes*)	**0.10**	**0.03**	**0.07 [0.03, 0.11]**	**<.001**	-0.01	0.01	-0.04 [-0.10, 0.03]	.33
Parental Drinking × Polygenic Risk Score	-0.03	0.02	-0.03 [-0.07, 0.01]	.11	0.00	0.01	0.00 [-0.06, 0.07]	.93
Parental Drinking × Friend Drinking	-0.03	0.02	-0.03 [-0.08, 0.02]	.26	**0.02**	**0.01**	**0.09 [0.01, 0.18]**	**.03**
Polygenic risk score	**0.11**	**0.03**	**0.08 [0.05, 0.12]**	**<.001**	**0.04**	**0.01**	**0.13 [0.07, 0.20]**	**<.001**
Friend drinking	**0.55**	**0.03**	**0.42 [0.38, 0.46]**	**<.001**	**-0.06**	**0.01**	**-0.21 [-0.28, -0.14]**	**<.001**
Polygenic Risk Score × Friend Drinking (G×E)	-0.00	0.02	-0.00 [-0.05, 0.04]	.91	0.01	0.01	0.03 [-0.04, 0.10]	.38
Model 2: Perceived friend disruptive behavior								
Sex (0 = *female;* 1 = *male*)	0.03	0.03	0.02 [-0.02, 0.06]	.34	**0.06**	**0.01**	**0.19 [0.13, 0.26]**	**<.001**
Sex × Polygenic Risk Score	0.02	0.02	0.02 [-0.02 ,0.06]	.34	0.00	0.01	0.00 [-0.06, 0.07]	.98
Sex × Friend Disruptive Behavior	0.01	0.02	0.02 [-0.03, 0.06]	.44	0.00	0.01	0.02 [-0.05, 0.10]	.56
Parental drinking (0 = *no;* 1 = *yes*)	**0.10**	**0.03**	**0.07 [0.03, 0.11]**	**.001**	-0.01	0.01	-0.03 [-0.10, 0.04]	.34
Parental Drinking × Polygenic Risk Score	-0.03	0.02	-0.04 [-0.08, 0.00]	.06	0.00	0.01	0.01 [-0.06, 0.08]	.74
Parental Drinking × Friend Disruptive Behavior	0.00	0.02	0.01 [-0.04, 0.05]	.85	0.01	0.01	0.04 [-0.05, 0.12]	.40
Polygenic risk score	**0.12**	**0.03**	**0.09 [0.06, 0.13]**	**<.001**	**0.04**	**0.01**	**0.13 [0.06, 0.19]**	**<.001**
Friend disruptive behavior	**0.36**	**0.03**	**0.30 [0.26, 0.34]**	**<.001**	**-0.06**	**0.01**	**-0.23 [-0.31, -0.16]**	**<.001**
Polygenic Risk Score × Friend Disruptive Behavior (G×E)	-0.00	0.02	-0.00 [-0.05, 0.04]	.96	0.00	0.01	0.02 [-0.06, 0.09]	.70

Notes: N = 8,906. Estimates significant at $p < .05$ are shown in **bold.** To account for population stratification, models controlled for the top 10 principal components, although results for these terms are not shown above for simplicity. Polygenic risk score results reported here are based on a $p < .50$ threshold, which was found to maximize predicted variance in adolescent drinking frequency; ancillary analyses across the range of polygenic risk score thresholds are available through author request. CI = confidence interval; G×E = gene–environment interaction.

Conditional latent growth curve models

Regarding models with perceived friend drinking (Table 2, Model 1), polygenic risk scores, perceived friend drinking, male sex, and parental heavy drinking were positively associated with adolescents' initial level of alcohol frequency at age 16 (i.e., intercept). Polygenic risk scores and male sex were also associated with increases in alcohol frequency from ages 16 to 20 (i.e., slope), whereas greater perceived friend drinking was associated with reductions in frequency across this period. Polygenic risk scores and perceived friend drinking did not interact in their associations with adolescents' initial level or rate of change in drinking frequency over time, after controlling for sex, parental heavy drinking, genetic principal components, and interactions of these covariates with the genetic and environmental risk terms.

Regarding models with perceived friend disruptive behavior (Table 2, Model 2), polygenic risk scores, perceived friend disruptive behavior, and parental heavy drinking were positively associated with adolescents' initial level of alcohol frequency at age 16 (i.e., intercept). Polygenic risk scores and male sex were also associated with significant increases in alcohol frequency from ages 16 to 20 (i.e., slope), whereas greater perceived friend disruptive behavior was associated with reductions in drinking frequency. Polygenic risk scores and perceived friend disruptive behavior did not interact in their associations with adolescents' initial level or rate of change in drinking frequency over time, after controlling for sex, parental heavy drinking, genetic principal components, and interactions of these covariates with the genetic and environmental risk terms.

Discussion

This study tested whether polygenic risks for adolescent alcohol use development were stronger in the presence of alcohol-specific and nonspecific peer environments. Within a large prospective sample, greater polygenic risk was associated with higher initial level of drinking at age 16 as well as steeper growth in drinking frequency from ages 16 through 20. Greater perceived friend drinking and disruptive behavior both were associated with higher initial level of drinking at age 16 as well as with decreasing rates of drinking frequency from ages 16 through 20. Contrary to study hypotheses, polygenic risk scores and perceived friend environments did not interact in their associations with drinking over time. Findings support the importance of both genetic and environmental factors in adolescent alcohol use development, while informing future developmental G×E research efforts.

Findings supported robust, albeit small, genetic associations with adolescent drinking. Consistent with increasing genetic influences across development (Kendler et al., 2008;

Rose et al., 2001), the maximally informative polygenic score explained 0.7% of the variance in adolescent alcohol use at age 16 and 2.4% at age 20. Although the mechanisms underlying such relations warrant further research, adolescents at heightened genetic risk may experience more positive subjective responses to alcohol (Enoch, 2014) and greater craving for alcohol (Agrawal et al., 2013), and/or possess more impulsive or other heritable personality traits (Niv et al., 2012) that drive escalations in drinking over time. Adolescents at greater genetic risk may also independently seek out alcohol and drinking opportunities after their initial drinking experiences (i.e., gene–environment correlation; Beaver et al., 2008; Harden et al., 2008), especially when alcohol is generally accessible within society.

The current study did not demonstrate significant developmental G×E effects. In contrast to a social control framework, genetic risks were not magnified in alcohol-promoting peer environments. This theoretically driven investigation tested peer environments modulating polygenic risks within a large prospective sample, controlling for key confounds (i.e., Sex × Friend Drinking; Parental Heavy Drinking × Friend Drinking) that ultimately explained adolescent drinking rather than G×E specifically. The current investigation replicates nonsignificant developmental G×E findings involving polygenic risks from two smaller samples (Li et al., 2017; Su et al., 2018), yet contradicts a recent twin study reporting stronger genetic risks in the presence of greater friend drinking from ages 13 to 17 (Zheng et al., 2019). Such discrepant findings may reflect generally larger heritability estimates among twin than polygenic risk studies (see Génin, 2020). In addition, peer environments may promote manifestation of genetic risks earlier in adolescence (as in Zheng et al., 2019) than were captured in the current investigation spanning ages 16 to 20. Social control G×E effects may be greatest amid variable peer drinking norms, limited access to alcohol outside the peer network, and varying opportunities to drink earlier in adolescence. Once drinking patterns become somewhat more established and alcohol readily accessible outside the peer network, any peer modulation of genetic risks may diminish. Ultimately, however, polygenic G×E influences in adolescent alcohol use development remain largely unknown. There is a clear need for theoretically driven study designs, especially those examining polygenic G×E influences across adolescence and within diverse samples, to resolve this literature.

Both perceived friend drinking and disruptive behavior were linked to adolescent alcohol use development, regardless of genetics. Adolescents surrounded by prevalent peer drinking and externalizing behavior may experience strong peer modeling effects, being more likely to normalize frequent drinking, receive and accept alcohol offers, participate in drinking games, and drink more frequently. Over time, however, greater initial friend drinking and disruptive behavior were associated with decreases in personal drinking through age 20. Although counterintuitive, a similar pattern in which friend substance use was positively associated with initial level of drinking yet negatively associated with its slope over the subsequent 6 years has been demonstrated (Li et al., 2017). Adolescents reporting that all of their friends drank at age 16 were only able to experience a maintenance or decrease in the number of drinkers within their peer network, rather than escalations in peer drinking that may promote increases in personal drinking. Nevertheless, it is important to recognize that peer environments have dynamic, reciprocal associations with alcohol use over time. Adolescents can match the drinking behavior of their peer network (i.e., peer socialization) as well as select into peer groups compatible with their personal drinking behavior and alcohol-related cognitions (i.e., peer selection; Burk et al., 2012; Curran et al., 1997). These reciprocal relationships warrant future investigations into polygenic modulation of both peer socialization and selection processes in adolescent drinking.

Several limitations should be considered. First, findings are based on observational data, and causal relationships should not be inferred. Second, this investigation assessed perceived rather than actual environments, and adolescents can overestimate their peers' drinking (Borsari & Carey, 2003; Perkins, 2002). Adolescents' perceptions of their friends' behavior may be arguably more important than their friends' actual behavior if incorrectly perceived and exaggerated by the adolescent, although it remains to be demonstrated to what extent actual compared with perceived friend drinking drives adolescent alcohol development. Relatedly, adolescents self-reported their drinking; although self-reported drinking has demonstrated reasonable reliability (Gruenewald & Johnson, 2006), potential motivations to over- or underreport use and/or memory inaccuracies may warrant externally validated measures in future efforts. Third, drinking frequency was modeled from ages 16 to 20 due to inconsistency in items across earlier time points, and G×E effects in early adolescence remain unknown. Fourth, missing data and attrition present concerns for the representativeness of the final sample. Although ancillary analyses suggested the significance of results were robust across those with and without complete data, systematic differences may have magnified associations of polygenic risk scores and/or perceived friend drinking with adolescent drinking. Fifth, although polygenic risk scores generally maximize explained variance relative to single gene approaches, the current polygenic risk score cannot speak to specific variants associated with alcohol use, and this liberal risk score calculated based on a high p value threshold likely included some genetic noise.

Last, findings are based on a restricted sample of White adolescents of moderate to high socioeconomic status in Great Britain who reported prevalent peer drinking and low peer disruptive behavior. Social control G×E effects may be

greater among adolescents in the United States and other countries where access to alcohol is more limited by legal restrictions (i.e., higher legal drinking age). Further, peer environmental effects likely vary considerably across cultures. Replication within samples of diverse racial/ethnic, socioenvironmental, and geographical location is crucial to assess generalizability in the timing and extent of any G×E effects.

This study tested developmental G×E effects on adolescent drinking within a large, prospective sample. Findings supported genetic and peer environment associations with drinking frequency across 5 years but did not find support for G×E effects, after controlling for potential confounding interactions. Future well-powered replication and generalization efforts are needed to examine any G×E effects contributing to adolescent alcohol use development across samples of diverse race, culture, developmental stage, and drinking behavior.

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